Table 4. Genetic alterations conferring hypersensitivity to Top1 poisoning in fission yeast:

Yeast Saccharomyces Pombe Humans Gene Effect Refs. **Function** Gene **Effect** Refs. Rhp54 HS (129) Homologous recombination (HR) RAD52 ? Rhp55 LS (129)Homologous recombination (HR) XRCC2 HS (219, 230, 234) Rhp22A LS (129)Homologous recombination (HR) XRCC3 HS (219)Rhp51 S (129)RecA homolog; Rad52 epistasis G. RAD51C HS (223)rad22 HS (247)Rec A homolog; functions with Mus81 RAD50 Rad50 HS (129)MRX/N complex; scaffold Mus81 S (129)3'-flap endonuclease with Eme1; MUS81 NS (137)meiotic recombination Eme1 (129)Partner for mus81 nuclease MUS81 ? RusA RS [a] (129)HJ resolvase Polynucleotide kinase phosphatase PNKP HS (115) Pnk1 S [b] (112)Rqh1 MS (98) Top3-associated helicase WRN HS (227-229)BLM HS (82)Chk1 S (155, 248)Checkpoint effector kinase CHK1 S (162, 165)Swi1 HS (249) Mating-type switching **TIMELESS**

Abbreviations for effect: HS, S, MS, and CS correspond to hypersensitivity, sensitivity, moderate sensitivity, and conditional sensitivity to camptothecin, respectively. NS: no hypersensitivity.

[a]: rusA suppresses hypersensitivity of $Mus81/Eme1^-$ but does not reverse sensitivity of $rqh1^-$; rusA also suppresses the lethality of double mutants for Mus81/Eme1 + rqh1 (129). RusA expressed in budding yeast partially suppresses hypersensitivity to CPT in Mms4-deficient cells (126).

[b]: *Pnk1*- cells are hypersensitive to CPT in the absence of additional defects, indicating difference from budding (see [a]) and importance of this pathway in fission yeast, which like mammals possesses a gene that has both 3'-phosphatase and 5'-kinase activity (*112*).